Review Article

Tibiotalocalcaneal Arthrodesis with Intramedullary Nails – Mechanobiological Background and Evolution of Compressive Technology

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Abstract

Tibiotalocalcaneal arthrodesis is a surgical procedure which involves fusion of the tibiotalar and subtalar joints to reduce patient pain, increase stability, and improve function. The success of this procedure largely depends upon the stability and apposition of the bone surfaces being fused. Intramedullary nails have long been used as a method of internal fixation during the tibiotalocalcaneal arthrodesis process to reduce micromotion and provide stability and compression across the joints. This review focuses on the mechanobiological processes and foundations of arthrodesis, along with the evolution of intramedullary nails used during arthrodesis. This evolution includes both material selection and, in particular, the ability of nails to provide compression across the fusing joints. This compressive evolution includes external compression, internal compression, and finally sustained internal compression as provided by the intramedullary nails.

Keywords: Bone Mechanobiology; Internal Fixation; Joint Fusion; NiTiNOL; Sustained Compression; Tibiotalocalcaneal Arthrodesis; Union

Abbreviations: CAD: Computer-Aided Design; CT: Computed Tomography, IM: Intramedullary mm: Millimeter; N: Newton; NiTiNOL: Nickel Titanium Naval Ordnance Laboratory; SCN: Sustained Compression Nail; TTCA: Tibiotalocalcaneal Arthrodesis; μ: Micro

Introduction

In many cases, tibiotalocalcaneal arthrodesis (TTCA) acts as a salvage procedure and alternative to amputation in nonbraceable neuropathic deformities, failed ankle arthrodesis, failed total ankle arthroplasty, talar osteonecrosis, and severe ankle and subtalar arthritis [1,2]. The goal of this procedure is to fuse the ankle and subtalar joints simultaneously leading to pain relief, stability, and a functional limb [3]. The purpose of this review is to examine the mechanobiological foundations of TTCA and the technological evolution of intramedullary (IM) nails used to provide fixation in TTCA procedures.

Discussion

Mechanobiological background

Mechanobiology is the study of how mechanical or physical stimuli regulate biological processes [4]. Julius Wolff was among the first to recognize the influence of mechanical forces on bone morphology and architecture, and in 1866 observed that trabecular trajectories within the proximal femur roughly align with directions of maximum stresses [5,6]. Wolff's Law states that mechanical inputs, creating functional and morphological changes in a bone, are followed by alterations of the bone's architecture and mechanical strength. Animal and cell culture models and their associated techniques (histology, radiography, mechanical testing, etc.) have been used to study the effects of mechanical inputs on biological responses, including bone repair, at multiple biological scales. Mechanobiological principles are relevant to TTCA with IM nails, because knowledge of micromovements and mechanical stresses, and how they stimulate bone cells leading to tissue adaptation, can be incorporated into development of new nail designs, leading to improved joint fixation and superior local healing conditions [7,8].

Bone Mechanobiology can be described at three levels in a "bottom up" perspective. The cellular level is at the bottom, as cells are the ultimate effectors of biological change. Cells are involved in mechanotransduction, which is the cellular process of converting external mechanical force inputs into biochemical responses [7]. These inputs have been reported to take a variety of forms, including direct stretch of the substrate upon which cells are bound, hydrostatic pressure, strain-induced electric streaming potentials, and mechanical strain due to fluid flow shear [5,7,9]. Fluid shear has generally been accepted as the most dominant input. The osteocytes, which are bone cells that inhabit the fluid-filled lacunacanalicular network connected by cellular processes, have been reported to be the primary mechanoreceptors in bone [5-7,9,10]. External forces create pressure gradients which induce flow of fluid, allowing osteocytes to "sense" mechanical loading via fluid shear. This fluid is driven back and forth through cyclic loading, causing strains and activating surface mechanoreceptors which initiate intracellular mechanotransductive signaling cascades. These cascades involve ion channels, integrins and the cytoskeleton, gap junctions and hemichannels, and primary cilia. Specific cascades involve activation of downstream targets in other known pathways that regulate bone growth or bone resorption and function, including osteopontin, Calcium, nitric oxide, prostaglandin E2, and RANKL.

Moving "up" to the tissue level of bone mechanobiology, much of the information obtained has come from in vivo animal models (rodents, sheep, etc.), in particular models of fracture repair. Loading during early healing stages impedes stabilization of injury sites, which is important for early bone matrix deposition [8,11-13]. High strain areas promote growth of fibrous tissue, which impedes and delays bone formation. Reduced bone formation is observed in cases of early loading, as rupture of newly forming vasculature can occur [14,15], and rigid, stable fixation enhances early bone formation [4,11,16]. Sustained compression in early stages of repair leads to mechanically stronger bone constructs at earlier time points, as direct intramembranous bone formation happens in cases of low stress and strain. Loading during later stages when matrix deposition and remodeling is occurring may enhance stabilization through formation or reorganization of osseous tissue, and dynamization allowing for cyclic loading enhances bone formation. However, lack of stable bony apposition delays or prevents fusion [17-20], as increased interfragmentary movement leads to significantly more fibrocartilage and a smaller number of vessels in the bone healing area. Additionally, gap formation prohibits fusion, as under comparable biomechanical conditions, gap-free fractures or small fracture gaps heal faster than medium-sized gaps (~2 mm), and large fracture gaps (~6 mm) do not experience bony union [21].

At the whole bone level, strain gauges allow measurement of bone strains in in vivo and benchtop models [7]. Frost studied the relationship between bone strain amounts and mechanobiological adaptations, leading to his Mechanostat Theory on Bone Adaptation [22,23]. Under this theory, 50-100 µstrain leads to disuse remodeling, as bone is removed through osteoclast activity, 100-1,000 µstrain represents naturally acceptable strain levels for maintaining bone, 1,000-1,500 µstrain is associated with modeling, as bone is added through activity of osteoblasts, 3,000-5,000 µstrain induces microdamage, which can be repaired over time in healthy individuals, and 25,000 µstrain causes abrupt fracture of bone. Bone strain levels induced by common activities include walking at 400 µstrain and running at 2,100 µstrain [24]. Note that vigorous running strains approach the microdamage region, such that stress fractures from intense running can occur. On the other hand, high frequency, low magnitude µstrain activities (i.e. muscle contraction during resting) can help to maintain bone mass [5,7]. Corresponding local loads of 300-700 N have been suggested for bone healing [24].

Evolution of compressive technology

An understanding of the importance of stability and mechanical control at the whole bone level has been around for hundreds of years, particularly in the area of fracture healing [13,25,26]. Knothe et al. presented a detailed account of the historical evolution of intramedullary fixation devices [25], which will briefly be summarized in part here. In the 1600's Conquistadors described use by Aztecs of resinous wooden pegs placed in the medullary canal of long bones to stabilize non-unions, while the 1800's to early 1900's brought medical journal reports of ivory and bone fixation pins or pegs to treat pseudoarthroses, but usage was problematic due to material resorption prior to healing. The early 1900's brought introduction of biologically inert materials, and radiography for surgical implantation and positioning assistance. As early as 1913 Groves recognized that bone-implant interface motion impedes fracture healing and may cause resorption. In the 1940's Kuntscher helped to introduce the modern concept of IM nailing for fracture stabilization with V-shaped and clover-leaf metal IM nails. In 1942 Maatz began reaming of the IM cavity to maximize contact between nail and bone and allow for larger nail use. In the Late 1960's, Kuntscher, Klemm, and Schellmann used early modern locking nails with the addition of transverse screws. Halloran, Grosse, and Kempf then introduced nail dynamization with nail slots. Finally, the 1990's saw increased use of titanium due to its stiffness being closer to cortical bone, high fatigue and yield strength, good biocompatibility, and superior imaging properties.

Arthrodesis is the surgical fusion of a joint for the purposes of obtaining pain relief, deformity correction, and stability [1,27,28]. Historically, Park is said to have performed one of the first arthrodesis procedures in 1781 of a tuberculous knee joint. Arthrodesis of the ankle was described by Albert in 1879 for treatment of paralytic equinus [29]. In 1882, Albert introduced the term ''arthrodesis'' after he started performing them to stabilize the feet and ankles of polio sufferers [27,29]. In 1906, Lexer used boiled cadaveric bone as an IM device [2]. In 1948, Adams reported the first case of TTCA with a metal IM nail [2], while in the 1950's Charnley pioneered compression arthrodesis of knee, shoulder, and

ankle using external fixation [28], with Ratliff following with his own ankle arthrodesis compression study [30]. In 1962, Kuntscher introduced the concept of locked retrograde nails for TTCA.

Charnley noted that compression helped eliminate shearing strains and gaps between the cut bone surfaces. Several mechanical factors have been associated with successful arthrodesis [1,29,31-33]; these include bony apposition with high contact area, primary stiffness and stability by rigid immobilization (limits micromotion between surfaces and promotes direct or primary bone healing with minimal callus/fibrous tissue formation), sufficient compression at desired fusion site (contributes to rigidity by neutralizing shear and bending forces and maintaining apposition), and load sharing between hardware and native bone (contributes to bone modeling once weight-bearing begins, and prevents fatigue failure of hardware in cases of non-union).

Successful TTCA requires a stable fixation method limiting micromotion of fusion surfaces, maintenance of desired multi-planar alignment, and apposition of well-vascularized bone. Compression, which contributes to all of these, is commonly provided by external fixators or intramedullary nails, and less frequently screws and plates. Benefits of external fixators include sustained compression throughout the healing process, and the option for use in complex ankle pathology and patients with suboptimal bone quality. Potential drawbacks include patient noncompliance and limited follow-up, increased patient pain or discomfort, pin tract infections and shaft fractures from pins, technical difficulty with time-consuming procedures, limited multiplanar/rotational stability in some studies, and high costs [31,34-36]. Benefits of IM nails include insertion with minimal soft tissue destruction, maintenance of overall multiplanar alignment, high primary stability, including axial, bending, and particularly rotational, and firm internal fixation reduces time for immobilization, along with the ability to be used in cases of severe deformity, gross instability, or salvage procedures [1-3,37]. IM nail drawbacks include potential for undesired axial motion or rotation if screws are not tight fit within nail holes, fatigue failure if stress shielding occurs, and screw loosening or motion [13].

IM nails used in TTCA in the modern era can generally be divided into three different classes or generations based upon capacity for compression [38,39]. 1st generation IM nails require surgeons to manually compress the fusion site by hammering a strike plate on the installation hardware. These early nails are considered "static" nails and simply offered calcaneal and tibial locking screws. 2nd generation IM nails were developed to a offer method to apply external compression. They used compression rods installed through the tibia and connected to the installation frame of the nail. Rods can either be installed through or above the nail and are subsequently removed once the nail has been successfully implanted. These nails can only apply intraoperative compression. 3rd generation IM nails incorporate internal compression mechanisms (generally internal axial screws). The goal of these nails is to help maintain compression during installation and instrument

removal. 3rd generation nails still offer external compression but have replaced external rods with compression apposition sleeves. The sleeve applies force directly to the calcaneus after the tibial screws have been inserted.

Comparisons of the varying nail generations have been performed both in benchtop and clinical settings. Muckley performed biomechanical testing with synthetic bone and reported that nails with compression exhibited greater multiaxial primary stiffness and contact surface area than nails without compression ability [31].

Additionally, Muckley performed a study of the primary stability of TTCA constructs using IM nails in a cadaveric model [32]. Internal compression nails were observed to be significantly stiffer in internal/external rotation than external compression nails, while compression nails overall were significantly superior in these respects than uncompressed nails. Berson reported on an IM nail cadaveric arthrodesis model comparing 1st generation IM nails with nail-mounted compression nails [40]. After removal of implantation fixturing, 1st generation nails lost all compression, while nail-mounted compression nails still lost approximately 40% of compression. Clinically, Pelton measured travel of dynamic locking screws within dynamic locking nails. The screws translated distally in nail slots an average of 2.3 mm due to impaction in 30 patients [41]. Finally, Taylor reported significantly faster TTC fusion and higher union rates for internal compression nails compared to nails without internal compression. However, there was no statistically significant difference after controlling for diabetes.

Reported clinical outcomes (such as union rates and functional restoration) vary considerably for TTCA patients with IM nail fixation, likely due to the variety of clinical indications, different nail types, evaluation method for union, and heterogeneity among patients [2]. Union rates have varied from 48% to 100%, with lower rates frequently associated with challenging patient and case factors including but not limited to tobacco or drug use, diabetes, neuroarthropathies, bulk bone defects, and revisions [2,27,37,42-46]. In particular, one study involving TTCA with IM nails and bulk femoral head allografts to treat bulk defects reported a 50% union rate, but that rate dropped to 0% for diabetic patients with bulk grafts [42]. Reported complication rates have varied from 21-80% [2,37,47], with hardware complications making up a significant proportion. As an example, incidence of bone healing complication in diabetic patients is believed to be high in foot and ankle surgeries [48-55]. In a case-control study of diabetic patients, approximately one out of four patients had one or more bone healing complications [56]. In that study, the authors found that the most significant factor associated with bone healing complication in diabetic patients was presence of neuropathy. The diabetic patients with neuropathy had four times the odds of having bone-healing complication than diabetics without neuropathy. Nonunion and complications following this salvage procedure can lead to amputation, which may compromise life-expectancy, quality of life, and create lifetime costs as high as $500,000 [57]. Additionally, patients with diabetic

foot disease fear major lower extremity amputation more than death [58].

One potential explanation for reported clinical problems following TTCA with IM nails, despite their theoretical fixation benefits, is a loss of fixation post-surgery. Most compression and stability assessments only report "Day 0" values despite arthrodesis being a spatiotemporal process that occurs over weeks or months. These assessments do not take into account any biological changes occurring during the bone healing process [13, 32]. Decreased nail-mediated compression can occur over time in vivo due to bone resorption, joint settling, and implant loosening [59, 60]. Bone loss can be greatest in the lower extremities, particularly the calcaneus, where fluid pressures decrease substantially with bed rest [6]. Challenging TTCA patients can have poor vascular, immune, and nutritional status, potentially increasing resorption. For example, in diabetic patients with neuropathy, lack of adequate neuropeptide release up-regulates osteoclastogenesis while down-regulating osteoblastic activities, resulting in bone resorption at the site of arthrodesis [61-64]. Therefore, a contact fixated by static compression can lose its stability once the bone resorption takes place in these high-risk patients. Bone resorption can lead to gap formation, resulting in loads being carried by implant hardware and stress shielding of bone, eventually causing hardware fatigue failure [24,26]. As even 3rd generation IM nails with internal compression may lose a high percentage of compression intraoperatively [40], it is possible that much more could be lost during the following weeks and months of the fusion process. Some have attempted to address this issue by combining use of IM nails with external fixators, which would provide torsional and bending resistance via IM nail and sustained compression via external fixator to close any gaps [65], as compression can continuously fill the gap created by the bone resorption to maintain stability throughout the course of bone healing. Colgrove reported 100% fusion of 26 consecutive ankles including patients with challenging conditions. However, this approach still presents the drawbacks of external fixators – long procedures, pin tract infections, patient noncompliance – while adding even higher costs with the combined price of both devices.

Some studies have investigated internal fixation using sustained compression nails or screws which incorporate springs, as a constrained spring can exert forces as it tries to recover an initial length. One such screw was reported to provide more compression in a simulated bone resorption benchtop model than a standard screw [60]. Another study reported on an IM nail which can sustain a dynamic compressive force by inclusion of a stretched spring within a nail outer body [24]. Matched pair cadaver testing in femurs revealed that compressive spring nails had greater compressive, rotational, and bending stiffness than standard nails. These nails generated 400N of force, corresponding to 400-2,400 μstrain at simulated fracture sites. However, downsides of spring compression include a limited diameter without losing bending and rotational strength of the outer body or exceeding the intramedullary canal space, and a generally linear relationship between force and deformation for basic spring designs, where

load applied by springs drops off quickly as springs unload. As such, these devices do not really apply a sustained compression, but rather a dropping compressive force with spring recovery.

An alternative method for applying compression that is sustained is through the use of NiTiNOL. NiTiNOL, an alloy consisting of approximately 50% (atomic) Nickel and 50% Titanium, was so named due to its development at the Naval Ordnance Lab, where it was first developed by Buehler and Wang in 1959 [66-68]. NiTiNOL can recover from deformations up to 8% strain – 10X more than traditional metals. The alloy is biologically safe and corrosion-resistant without cytotoxic, allergic, or genotoxic activity. Additionally, NiTiNOL forms a passive Ti oxide layer that acts as a physical barrier to nickel oxidation and protects bulk material from corrosion, providing a protective effect for those with nickel allergies. The shape-change capacity of NiTiNOL is potentially beneficial for a variety of applications. The shape-change, called the pseudoelastic or superelastic effect [66,67,69], is largely possible because NiTiNOL presents two crystallographic phases, austenite and martensite. Deformation causes transformation from stable elastic austenite to unstable pseudoelastic martensite, and the stress over which this transformation occurs is approximately constant. The martensite is easily deformed, reaching large strains (~8%), which are recoverable. The shape and phase change of NiTiNOL can be mechanically-induced and occur at room temperature. In comparison, early NiTiNOL devices utilized the shape-memory effect of NiTiNOL, which requires martensitic deformation or stretching at cooled temperatures. Martensite is unstable when uncooled, so it tries to transform back into stable austenitic material and recover its original shape. NiTiNOL devices using shape-memory generally have to be kept cold in liquid nitrogen, then quickly be placed into desired position before they heat up and try to recover their undeformed shapes. NiTiNOL devices will exert a sustained force if they are prevented from returning to their original shape, and this force is largely constant during shape recovery.

Early research into NiTiNOL devices for orthopaedic use was performed by Hughes in the 1970's on behalf of the U.S. Army Medical Research and Development Command [70]. Strain gauges were applied to osteotomized sheep femora with attached NiTiNOL plates, which confirmed compressive loading of the bones and closure of bone gaps during recovery of the stretched NiTiNOL. However, Hughes found that NiTiNOL was an extremely difficult material to machine and shape, which at the time prevented its widespread adoption. However, he provided design suggestions for devices made with NiTiNOL, which included employing a fairly large device stretch by extending the length of the strained zone for larger total stretch available, reducing the cross sectional area of the portion of the device that is strained to lessen the recovery stress to bone-compatible levels, and employing a telescoping or sliding piece within another rigid housing to provide combined bending and torsional strength that the thin NiTiNOL component would not provide. With recent improvements in NiTiNOL manufacturing, devices incorporating NiTiNOL have included

cardiovascular stents and filters, surgical instruments, glasses frames, bone plates, and staples [68, 69,71]. Studies document early use including staples applied in treating patellar fractures and in first metatarsophalangeal joint arthrodesis, and staples continue to be one of the most common NiTiNOL orthopedic devices.

Despite the potential benefits of sustained compression in orthopaedic procedures such as TTCA, IM nails incorporating NiTiNOL have been lacking. In 2002 Kujala investigated IM "nails" for correction of deformities by implanting straightened NiTiNOL pins into rat femurs. These pins exerted bending forces post-implantation as they attempted to return to their original curved shape. These forces led to bone bending, including cortical thickening on the compressive loading side [72]. In 2004 Firoozbaksh performed a similar study using straightened NiTiNOL rods in tibiae of rabbits to create bent bones [73]. Simple one-piece NiTiNOL fixation devices have been used successfully for small bone arthrodesis application [74,75], however, actual NiTiNOL IM nail clinical usage remained lacking despite potential benefits due to the extraordinary difficulty in melting, processing, and machining the alloy into complex shapes while maintaining its desired pseudoelastic properties.

Recently, a novel IM nail incorporating an internal NiTiNOL component (DynaNail®, MedShape, Inc.) was made available clinically [76,77]. This sustained compression nail (SCN) features an elongated thin cylindrical NiTiNOL compressive element housed within a more traditional titanium cylindrical outer nail body, and proximal and distal screw slots similar to other nails. In addition to allowing more traditional manual joint compression, during surgery the element is stretched 6 mm and secured in its extended length by screws through the calcaneus distally and tibia proximally. The element is then released, thus creating a sustained compressive load across both the tibiotalar and talocalcaneal joints for as long as the element remains elongated. Absent the stretching of the compressive element, the surgical technique with this nail is similar to more traditional, prior generation IM nails for TTCA [76]. This element-provided compression is retained during potential bone resorption at the joint surfaces or joint settling which may occur post-operatively during the arthrodesis process. If this occurs, the distal screws will shift proximally within slots, along with the connected calcaneus [45,77-79].

Given that the SCN's distal screws are in slots from the time of surgery, dynamization is possible from the day of surgery, rather than needing a completely separate surgery later to dynamize screws [44], yet the presence of the sustained compression provides initial stability which would be absent in a traditional IM nail dynamized during initial surgery. Immediate dynamization plus sustained compression allows for load sharing with the bone during weight bearing, even with resorption, as loads pass from one connected bone to another, while the dynamized compliant hardware only sustains a small portion of the load [80,81]. Other IM nails can stress shield the bone prior to dynamization, potentially leading to hardware fatigue failure prior to union. Prior studies

have emphasized the importance of dynamization to fusion, particularly for delayed union patients, going so far as to state that dynamization was "a necessary continuum" and "treatment augmentation, not treatment failure" for TTCA [44]. In addition, it is more difficult, generally, for high-risk patients to be compliant with the non-weight bearing status following arthrodesis procedures due to decreased balance, athleticism and increased body weight. In case of premature weight bearing or destabilizing forces at the arthrodesis site, stability achieved by static compression can be lost with small amount of displacement. On the other hand, a construct stabilized by dynamic compression can maintain its compression via a "recoil" mechanism even with some accidental displacement.

Benchtop studies comparing the biomechanics of the SCN and prior-generation IM nails have been performed using synthetic bone models with simulated resorption or gap formation [38,39,77,81]. These studies assessed both nail-mediated compressive and torsional loads. Simulated bone resorption of 1 mm led to a 90% reduction in compressive loads for intramedullary nails commonly used for TTCA lacking a sustained compression mechanism, whereas the SCN continued to compress beyond 6 mm of simulated resorption. The majority of the SCN's sustained compressive loads also fell within the range noted to be associated with bone healing [24]. Additionally, a substantial drop in torsional resistance was observed in prior generation nails with as little as 0.25 mm of simulated resorption, as loss of compression is associated with loss of frictional forces to resist rotation. Additional evaluation of the SCN was performed in a finite element analysis model [82]. CT data was used to create CAD models of the tibia, talus, and calcaneus, which were combined with device CAD files of the TTCA hardware. Static or non-dynamized IM nails were shown to stress shield forces from the bone, transferring only 17% of forces during simulated weight-bearing to the bone. Comparatively, the axial compliance of the SCN's dynamized compressive element allowed transfer of 67% of forces across the bone during simulated weight-bearing.

Clinically, positive results have been reported for patients treated with the SCN, including high-risk cases with multiple co-morbidities. Hsu et al. reported successful TTC union in an ankle fracture patient that failed ORIF who continued with a one-pack-per day smoking habit during the arthrodesis process [76]. Kruelen et al. described a case series of six patients with bulk defects that were treated with a synthetic bulk spacer and SCN [83]. Complete fusion was observed for all patients on radiographs, as early as 4-6 weeks, with an average of 8 weeks postoperatively. Kildow et al. tracked the recovery of the compressive element in fifteen patients on radiographs over an average of 195 days of follow-up [78]. They observed an average of 5.58 mm of migration, with 86% of the observed recovery occurring within the first 40 days postoperatively, suggesting the importance of sustained compression throughout this time period. Latt et al. reported a case series of two revisions, with one patient being diabetic and the other having Charcot neuroarthropathy [77]. Both went on to union as assessed by CT. Conklin et al. described two patients that experienced failed total ankle replacement who were converted

to TTCA with the SCN and bulk femoral head allografts [79]. Both patients experienced CT-assessed union of all joints. Ford et al. presented a retrospective case series of 33 TTCA patients treated with the SCN [45]. Overall, 91% of arthrodesis surfaces united, as assessed by CT. They additionally observed that the element recovered an average of 3.9 mm as assessed in post-operative radiographs, with the majority of the recovery occurring within the first two weeks of surgery. Lachman et al. reported results from two bulk defect patients following severe talar avascular necrosis, one of which was treated with SCN plus bulk femoral head allograft and the other treated with SCN plus 3D-printed synthetic cage [84]. Both patients went on to union. Finally, Steele et al. reported results from a retrospective Level III comparative study in which patients underwent TTCA with either a SCN (n = 50) or a non-dynamized IM nail (n = 36). They found that SCN patients had a higher fusion rate, with fusions occurring 3.9 months faster, than the non-dynamized nail group. These superior results were obtained despite the SCN group being used significantly more often in patients with known risk factors for non-union. Additionally, patients in the SCN group required significantly less supplemental fixation hardware than patients in the non-dynamized nail group.

Conclusion

These benchtop, modeling, and clinical results as a whole suggest that the SCN, capable of providing immediate dynamization and sustained joint compression throughout the TTCA process, can produce favorable clinical outcomes in accordance with foundational mechanobiological principles. Future studies on the continued evolution of IM nail technology for TTCA should assess how variations in amounts and timing of sustained compressive loads affect the arthrodesis process.

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None

Conflicts of Interest

K.M. Dupont is an employee of MedShape, Inc. and owns stock/stock options in MedShape, Inc. N. Shibuya is a paid consultant of MedShape, Inc. and owns stock options in MedShape, Inc. J.T. Bariteau is a paid consultant of MedShape, Inc. and holds stock options in MedShape, Inc.

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